Intake of Carotenoids and Retinol in Relation to Risk of Prostate Cancer

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Background: **Several human studies have observed a direct association between retinol (vitamin A) intake and risk of prostate cancer; other studies have found either an inverse association or no association of intake of β-carotene (the major provitamin A) with risk of prostate cancer. Data regarding carotenoids other than β-carotene in relation to prostate cancer risk are sparse.** ***Purpose:*** **We conducted a prospective cohort study to examine the relationship between the intake of various carotenoids, retinol, fruits, and vegetables and the risk of prostate cancer.** ***Methods:*** **Using responses to a validated, semiquantitative food-frequency questionnaire mailed to participants in the Health Professionals Follow-up Study in 1986, we assessed dietary intake for a 1-year period for a cohort of 47 894 eligible subjects initially free of diagnosed cancer. Follow-up questionnaires were sent to the entire cohort in 1988, 1990, and 1992. We calculated the relative risk (RR) for each of the upper categories of intake of a specific food or nutrient by dividing the incidence rate of prostate cancer among men in each of these categories by the rate among men in the lowest intake level. All *P* values resulted from two-sided tests.** ***Results:*** **Between 1986 and 1992, 812 new cases of prostate cancer, including 773 non-stage A1 cases, were documented. Intakes of the carotenoids β-carotene, α-carotene, lutein, and β-cryptoxanthin were not associated with risk of non-stage A1 prostate cancer; only lycopene intake was related to lower risk (age- and energy-adjusted RR = 0.79; 95% confidence interval [CI] = 0.64-0.99 for high versus low quintile of intake; *P* for trend = .04). Of 46 vegetables and fruits or related products, four were significantly associated with lower prostate cancer risk; of the four—tomato sauce (*P* for trend = .001), tomatoes (*P* for trend = .03), and pizza (*P* for trend = .05), but not strawberries—were primary sources of lycopene. Combined intake of tomatoes, tomato sauce, tomato juice, and pizza (which accounted for 82% of lycopene intake) was inversely associated with risk of prostate cancer (multivariate RR = 0.65; 95% CI = 0.44-0.95, for consumption frequency greater than 10 versus less than 1.5 servings per week; *P* for trend = .01) and advanced (stages C and D) prostate cancers (multivariate RR = 0.47; 95% CI = 0.22-1.00; *P* for trend = .03). No consistent association was observed for dietary retinol and risk of prostate cancer.** ***Conclusions:*** **These findings suggest that intake of lycopene or other compounds in tomatoes may reduce prostate cancer risk, but other measured carotenoids are unrelated to risk.** ***Implications:*** **Our findings support recommendations to increase vegetable and fruit consumption to reduce cancer incidence but suggest that tomato-based foods may be especially beneficial regarding prostate cancer risk. [J Natl Cancer Inst 1995;87:1767-76]**

Throughout the Western world, prostate cancer is a large and growing problem. Without reductions in incidence or improvements in treatment, about 40 000 men in the United States will die annually from this malignancy by the year 2000 (*1*). The success in treating advanced prostate cancers remains poor, drawing attention to dietary factors that may influence risk of this malignancy, particularly animal fat, retinol, and carotenoids (*2,3*). Adequate levels of vitamin A or retinol are necessary for the normal control of both cellular differentiation and proliferation (*4*), and various retinoids have displayed the ability to inhibit carcinogenesis in animal models (*5*), including prostate cancer (*6*). However, in some experimental studies retinoids have enhanced carcinogenesis (*7,8*), and several human studies have found a direct association between retinol intake and risk of prostate cancer, particularly among men aged 70 years or older (*9-13*).

In contrast to dietary retinol, intake of β-carotene or provitamin A has been either inversely associated (*14-16*) or unassociated with risk of prostate cancer (*2*). In addition to being converted into vitamin A, β-carotene might influence carcinogenesis by reducing free radical damage (*17*) or by enhancing immunologic function (*18,19*). Although work has focused on β-carotene, more than 500 types of carotenoids exist in nature. The most common carotenoids include α-carotene, lycopene, lutein, and β-cryptoxanthin in addition to β-carotene. Epidemiologic data regarding specific carotenoids (other than β-carotene) and risk of prostate cancer are sparse because values for levels of carotenoids in foods have only recently become available (*20*). However, the study of food items or groups that

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